

Molecular Dynamics Simulations of Peptide Nucleic Acid at Lipid Bilayer

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Lipid molecules have hydrophilic part in addition to being largely hydrophobic. This amphiphilic character of the molecules makes them a key building block of cell membranes. As a result of the opposite tendencies, lipid molecules spontaneously form clusters, such as micelles (“monolayer” spheres), bilayers, or vesicles. Studies of lipid bilayers are important for our understanding of cell membrane’s behavior and functionality.

Peptide nucleic acid (PNA) is a lab-created analogue of DNA, in which the nucleic bases (adenine, guanine, thymine and cytosine) are attached to a pseudopeptide backbone. PNA can hybridize to its complementary DNA target in a sequence dependent manner. Unlike most of oligonucleotides analogues, PNA binds very tightly to double-stranded DNA as well. Because of this property, PNA molecules are intensively exploited in gene chemistry – a novel, straightforward, and versatile approach for permanently attaching proteins, peptides, fluorophores, and other molecules to plasmid DNA without interfering with transcriptional activity. PNA molecules have both polar and nonpolar parts – they are still hydrophobic but to some degree dissolve in water. In a system containing water, lipid clusters, and PNA molecules the synthetic nucleic acid adsorbs at the lipid – water interface because of its limited solubility.

Recently, a new potential application of PNA emerged in a minimal protocell design presented by Rasmussen and Chen [1]. The minimal protocell able to utilize resources, grow, self-replicate and evolve could be as simple as a small lipid aggregate acting as a container by anchoring a PNA molecule on its exterior. In such a protocell, light-driven metabolic processes could synthesize lipids and PNA, with the PNA acting as both an information carrier and as a catalyst, leading to a spontaneous growth of the protocell. Lipid clusters in water are thermodynamically stable below some critical size only; therefore the growing protocells would divide

as soon as they become large enough, giving next generation of the protocells. Research of the simplest self-reproducing nanosystem will not only create the basis for a revolutionary and powerful technology with multiple applications, but also provide new insights into the origins of life on Earth.

Molecular dynamics (MD) computer simulation is a powerful and suitable method for modeling the phenomena on the molecular level. In our research we exploit two freeware software packages designed for MD simulation and visualization: NAMD [2] and VMD [3]. The simulated system is shown in Fig.1. The results of

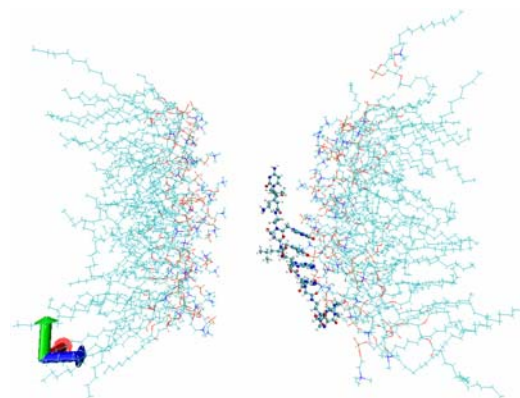


Fig.1. PNA molecule composed of six bases (CGTACG) in water between two lipid (DPPC) layers. Water molecules are invisible to make it more readable. Note that the PNA molecule is attached to one of the lipid-water interfaces.

our simulations suggest that PNA molecules indeed adsorb at the lipid-water interface [4]. The change of the system free energy associated with adsorption of the small PNA molecules at the lipid-water interface is on the order of several kT units per PNA molecule. The mean force acting between the PNA molecule and the lipid-water interface, as well as the free energy profile of the system is presented in Fig.2. The main driving force of adsorption and the final position of the PNA molecule in the simulated system depend on the hydrophobicity of the molecule. In the case of PNA molecules with charged terminal groups the main driving force of adsorption is the electrostatic attraction between the charged groups of the molecules and the charged heads of lipids. The main driving force of adsorption of PNA molecules with neutral termini is the hydrophobic interaction of the non-polar PNA groups with water. In this case the hydrophobic parts of the PNA molecule sink into the organic interior of the bilayer,

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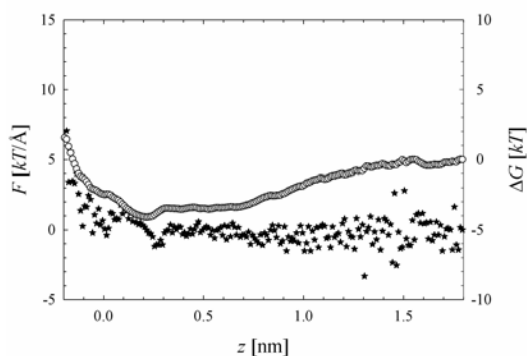


Fig.2. Free energy profile and mean force between PNA molecule with neutral termini and lipid-water interface. Stars denote the mean force, circles the free energy change.

therefore the mean distance of this molecule from the interface is smaller by a few angstroms than that of the PNA molecule with charged termini.

Acknowledgements

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